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RADIUM

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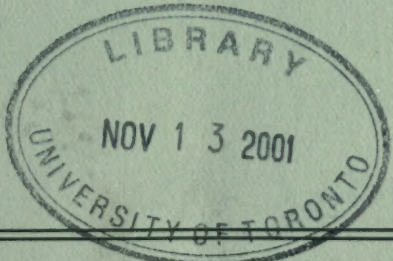
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APRIL, 1914

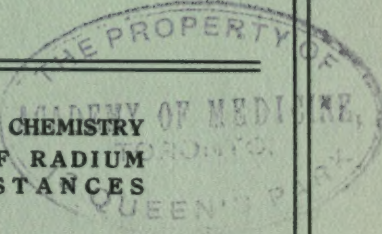
No. 1

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A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY
PHYSICS AND THERAPEUTICS OF RADIUM
AND RADIO-ACTIVE SUBSTANCES



RADIUM

A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY, PHYSICS AND
THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES.

Edited and Published by Charles H. Viol, Ph. D. and William H. Cameron, M. D.,
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VOL. III

APRIL, 1914

No. 1

INFLUENCE OF INTRAVENOUS INJECTION OF SOLUBLE RADIUM SALTS IN HIGH BLOOD PRESSURE.

By FREDERICK PROESCHER, M. D.

The action of the radium, especially its salts, upon the circulatory system and its function is very little known. *Plesch* has shown that by injection of 1/10 milligram of radium bromide in the jugular vein of the rabbit the systolic contraction of the heart is diminished and the blood pressure lowered. By means of the plethysmograph he found that the pulse pressure amplitude almost disappears and the action of the heart is reduced to a minimum. After a short time the heart recovers. The action of the radium is only temporary and without harm to blood pressure or pulse amplitude. The pulse frequency only seems to be diminished for a longer period. This phenomenon can be repeated to a lesser degree by repeated injections of smaller quantities of radium salts in the same animal. The experiment shows that radium acts at once upon the heart, and the effect is directly proportional to the quantity of radium. *Loewy* found after the intravenous injection into dogs of a radium solution of 1,000 m. u. (equal to about 0.4 microgram radium—a relatively small dose) that the systolic pressure was increased in one case, remained without change in four cases and was lowered in four other cases. In further experiments *Loewy* found the volume of the lung and brain showed an increase. *Loewy* concludes, therefore, that these experiments show a direct effect of the radium upon the vaso motors.

The effect of the radium emanation upon the circulatory system of human beings was investigated by *Plesch* and *Loewy*. They found that by inhalation of a low concentration of radium emanation (8 m. u. per liter) in the majority of the cases (8 out of 10 cases) the maximal pressure was lowered, in four also the minimal pressure. No increase of blood pressure was found in any instance. The respiratory metabolism, as well as the oxygen capacity of the arterial and venous blood, showed no change.

As I have demonstrated in previous communications, the blood pressure was lowered in the majority of the polyarthritis cases after injection of 50 to 300 micrograms of radium (element).

The blood pressure lowering properties observed in the cases after the intravenous radium salt injections suggested the use of radium in high blood pressure. Before reporting the results of these experiments I wish to refer briefly to our knowledge of the etiology of high blood pressure. The cases of hypertension we can group in three classes:

- 1st. Cases which are due to or followed by chronic nephritis.
- 2nd. Cases which are the result of organic cardiac lesions.
- 3rd. Cases which are either nephritic or of cardiac origin, idiopathic hypertension.

Sclerosis of blood vessels alone does not increase blood pressure. Probably the most important factor in hypertension are changes in the kidney. In cases with blood pressure over 200 mm. careful histological examination of the kidney shows a certain form of nephritis. Changes in the kidney are less frequent in patients with pressure below 180 mm. With our present chemical and microscopic methods we cannot in all cases of high blood pressure determine whether there is a serious involvement of the kidney or not. With further progress of our knowledge of the finer morphology of the kidney we will probably detect changes which cannot be seen at present. The functional kidney tests show only the grosser lesions. The structure of the kidney may be so modified that it increases the blood pressure, but still takes care of the waste products. If renal changes are the main factor in high blood pressure, then how are we to explain in what manner the high blood pressure is produced? The old theories of *Cohnheim* and *Traube* that mechanical interference of the blood flow in the kidney should be responsible for the increased blood pressure could not be experimentally confirmed. The hypertrophy of the heart in such cases is secondary. The retention of the waste products ordinarily eliminated via the kidney was also made responsible for the increased blood pressure, but none of the substances isolated from the urine has had a pressure action when injected into animals. It is not certain whether the nephrolysin has any effect upon the kidney. It was further thought that the suprarenal capsule through an increased output of adrenalin had an influence on the blood pressure. This seems to be confirmed by *Vaquez*, who found in cases of hypertension a hyperplasia of the suprarenal capsule, but his findings could not be proved by other investigators.

So far an increase of adrenalin in the blood serum of cases of high blood pressure could not be demonstrated. In conclusion we may say that we have no definite knowledge of the substance increasing the blood pressure, but it may be of a toxin nature. That such toxic substances are present in blood serum of cases of hypertension I was able to demonstrate in the blood serum of a case of idiopathic high blood pressure (systolic B. P. 230). Five cc. of the blood serum of this patient killed guinea pigs by intraperitoneal injection in 12 to 15 hours. The toxicity of the serum could be destroyed by heat at 60° C. for one-half hour. Control experiments with serum of human with normal blood pressure had no effect.

The serum of cases of high blood pressure caused by primary heart lesions was entirely atoxic for guinea pigs. These few experiments are not sufficient to draw any definite conclusions, but might throw light on the etiology of certain cases of hypertension. As long as we have no proper understanding of the different etiology of the hypertension, the therapy is purely symptomatic, and the few substances which are at present used for lowering the blood pressure, as nitroglycerine, the nitrites, etc., have only a temporary effect. Of the radioactive substances which are at present used we may mention thorium X, which by intravenous application, according to *Plesch* and *Falta*, will lower the blood pressure for a longer period. The objection to thorium X is its toxicity, which causes, in high dosage and prolonged use, toxic enteritis because of its retention (almost to 80%) within the organism. From our experience we know that the intravenous injection of radium salts in large doses and given over a longer period is without untoward effect and may replace the thorium X injection for lowering the blood pressure.

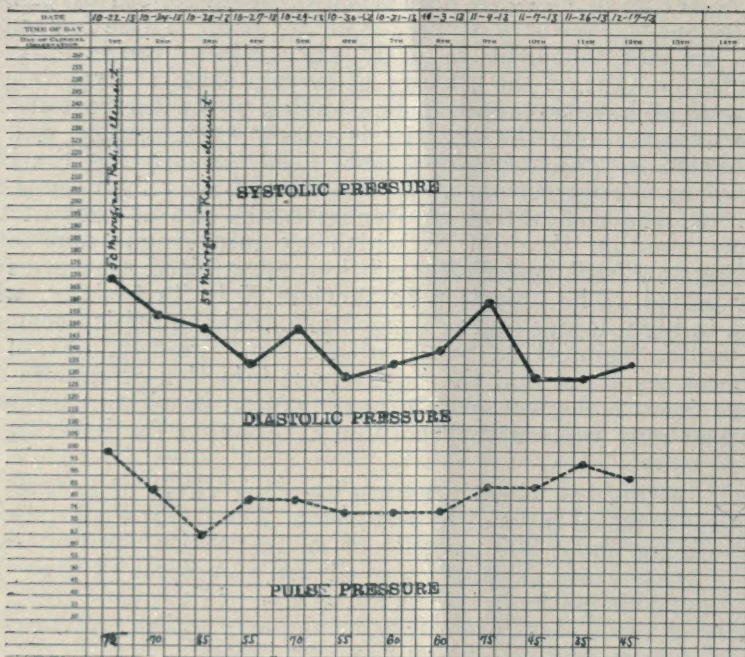
For testing the blood pressure lowering effect of radium salt we tried it in seven cases of hypertension. These cases were selected by examining about 200 patients of an institution for the insane. None of these cases exhibited any clinical symptoms of high blood pressure and the patients had no knowledge of their condition. The histories of these cases are rather incomplete, as the patients could not give a clear history of any previous illness.

CASE No. 1—Male, Age 70 Years.

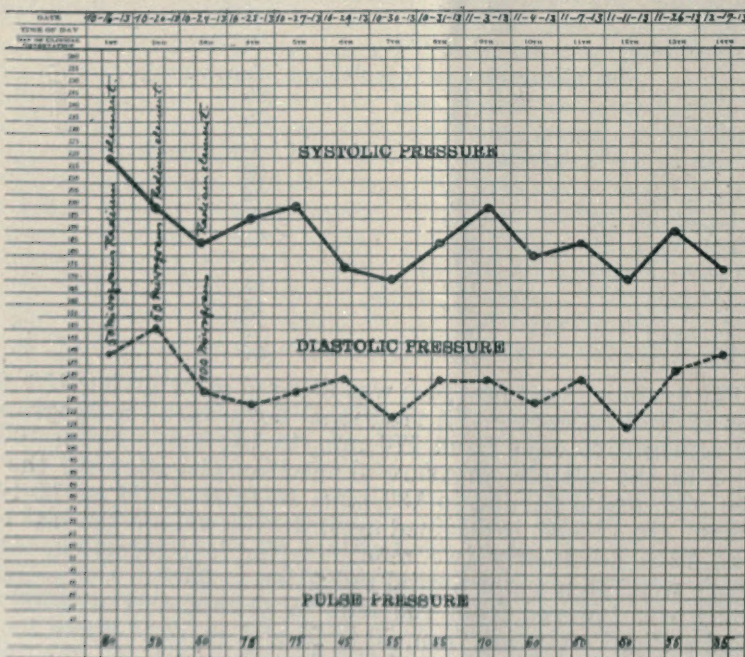
Chronic myocarditis, sclerosis of the peripheral arteries. No albumen or casts in urine.

Date	Systolic	Diastolic	Pulse Pressure
10-22-13	170 mm.	100 mm.	70
50 micrograms radium element intravenously.			
10-24-13	155	85	70
10-25-13	150	65	85
50 micrograms radium element intravenously.			
10-27-13	135	80	55
10-29-13	150	80	70
10-30-13	130	75	55
10-31-13	135	75	60
11- 3-13	140	75	60
11- 4-13	160	85	75
11- 7-13	130	85	45
11-26-13	130	95	35
12-17-13	135	90	45

The systolic blood pressure was lowered after giving 100 micrograms of radium element in fractional doses of 50 micrograms on three consecutive days from 170 mm. to 135 mm. From 10-27-13 to 11-7-13 the systolic pressure showed an elevation on the 29th to 150 mm. and a decline to 130 mm., to raise again on 11-4-14 to 160 mm. On 11-7-13 it declined again to 130 and on the last observation, 12-17-13, nearly two months after last injection, systolic pressure was 135 mm., or a total reduction of 35 mm. The diastolic pressure was lowered from 100 mm. to 80 mm. From 10-27-13 it showed a slight elevation from 80 to 85 and on 12-17-13 an increase to 90, a reduction of 10 mm. from first observation. The lowest pulse pressure was observed 11-7-13, being 35 mm., on 12-17-13 it



Blood Pressure Chart Case No. 1.



Blood Pressure Chart Case No. 2.

was 45 mm., being a total reduction of 30 mm. during the period of observation.

CASE No. 2—Male, Age 56 Years.

History of lead poisoning many years ago. At present time heart slightly enlarged, particularly left ventricle. Sclerosis of the peripheral vessels. Repeated examination of urine showed neither albumen or casts.

Date	Systolic	Diastolic	Pulse Pressure
10-16-13	220	140	80
	50 micrograms radium element intravenously.		
10-20-13	200	150	50
	50 micrograms radium element intravenously.		
10-24-13	185	125	60
	100 micrograms radium element intravenously.		
10-25-13	195	120	60
10-27-13	200	125	75
10-29-13	175	130	45
10-30-13	170	115	55
10-31-13	185	130	55
11- 3-13	200	130	70
11- 4-13	180	120	60
11- 7-13	185	130	50
11-11-13	170	110	60
11-26-13	190	135	55
12-17-13	175	140	35

The systolic pressure in this case was lowered immediately following the administration of 200 micrograms of radium element given in divided doses of 50, 50 and 100 micrograms from 220 mm. to 185 mm. The lowest systolic pressure after the injection of radium was observed fourteen days later, 10-30-13, to 170 mm. The final observation, on 12-17-13, showed the systolic blood pressure down to 175, being a total decrease of 45 mm. The diastolic pressure decreased immediately after the radium injection from 140 mm. to 125 mm. and reached its lowest mark on 11-11-13, being 110. From 11-11-13 to 12-17-13 there was an increase in the diastolic pressure to 140 mm., being the same as at the beginning of observation. The lowest pulse pressure was observed 12-17-13, being 35, or a total decrease of 45 mm.

CASE No. 3—Male, Age 72 Years.

Chronic myocarditis, sclerosis of peripheral arteries. No albumen or casts in urine.

Date	Systolic	Diastolic	Pulse Pressure
10-21-13	195 mm.	100 mm.	95 mm.
	50 micrograms radium element intravenously.		
10-22-13	160	80	80
	50 micrograms radium element intravenously.		
10-24-13	145	75	70
10-25-13	135	90	45
	50 micrograms radium element intravenously.		
10-27-13	120	80	40
10-29-13	125	75	50
10-30-13	115	75	40
10-31-13	130	75	55
11- 3-13	120	70	50
11- 4-13	140	75	65
11- 7-13	170	85	85
11-26-13	135	70	60
12-17-13	135	100	35

The systolic blood pressure, after giving 150 micrograms of radium element in divided doses, was lowered in four days from

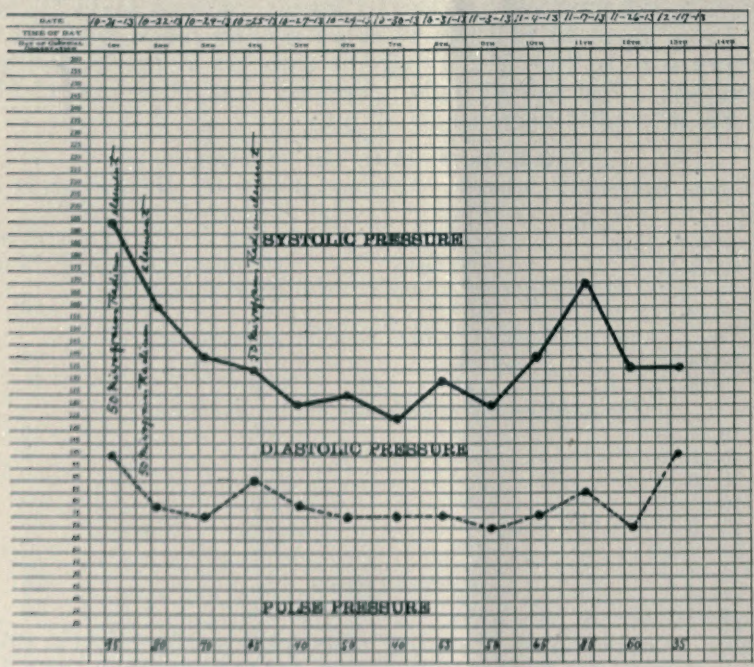
195 mm. to 120 mm., from 10-27-13 to 11-3-13 it showed tendency to slight elevation, an increase from 11-3-13 to 11-7-13 to 170 mm. was noted. The final examination on 12-17-13 showed the systolic pressure to be 135 mm., being a total reduction of 60 mm. The diastolic blood pressure was lowered during the first four days from 100 mm. to 80 mm., from 10-27-13 to 11-7-13 it showed a slight variation, the lowest being 70 mm. on 11-3-13. Increasing again to 100 mm. on 12-17-13, being the same as at the beginning of observation. The pulse pressure showed its greatest reduction on 12-17-13, 35 mm., being a total reduction of 60 mm.

CASE No. 4—Male, Age 60 Years.

Slight hypertrophy of left ventricle. Slight sclerosis of peripheral arteries. No albumen or casts found in urine.

Date	Systolic	Diastolic	Pulse Pressure
10-18-13	160	95	65
10-20-13	50 micrograms radium element intravenously.	165	90
10-22-13	50 micrograms radium element intravenously.	160	95
10-25-13	50 micrograms radium element intravenously.	150	95
10-27-13	100 micrograms radium element intravenously.	150	85
10-29-13		145	75
10-30-13		140	75
11- 4-13		135	80
11- 7-13	50 micrograms radium element intravenously.	140	80
11-11-13		140	90
12-17-13		155	105

After giving 250 micrograms radium element intravenously in divided doses of 50, 50, 50 and 100 micrograms the systolic blood



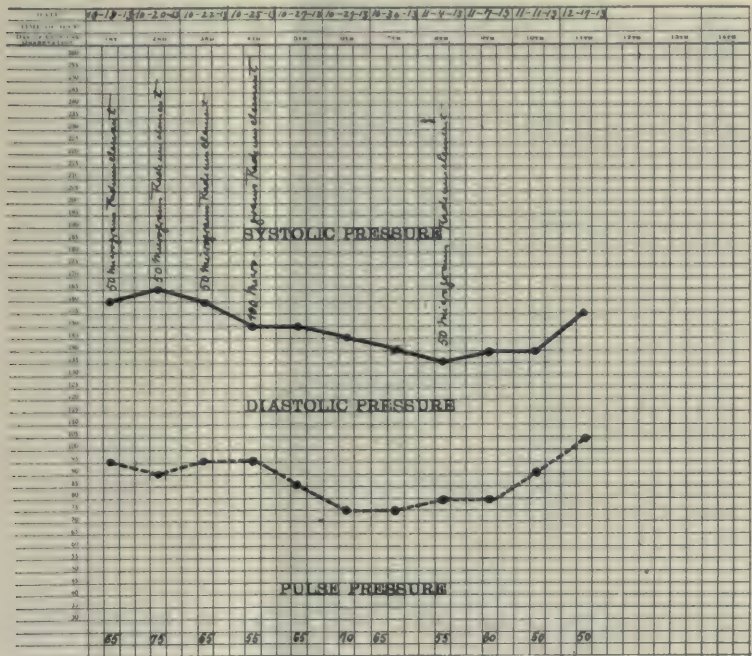
Blood Pressure Chart Case No. 3.

pressure was reduced from 160 mm. to 150 mm. within nine days after the first administration of radium. The lowest systolic blood pressure was observed 11-4-13, being 135 mm. After giving 50 micrograms more there was an increase to 140 mm. Upon final examination, 12-17-13, the systolic blood pressure was 155 mm., being only 5 mm. lower than at the beginning of observation. The diastolic pressure was reduced during the first nine days from 95 mm. to 85 mm. The lowest diastolic pressure was observed 10-29-13, being 75 mm., gradually increasing to 105 mm., 12-17-13, at time of last examination, being 10 mm. higher than at the beginning of observation. The lowest pulse pressure was noticed on 11-11-13 and 12-17-13, 50 mm., being a total reduction of 15 mm.

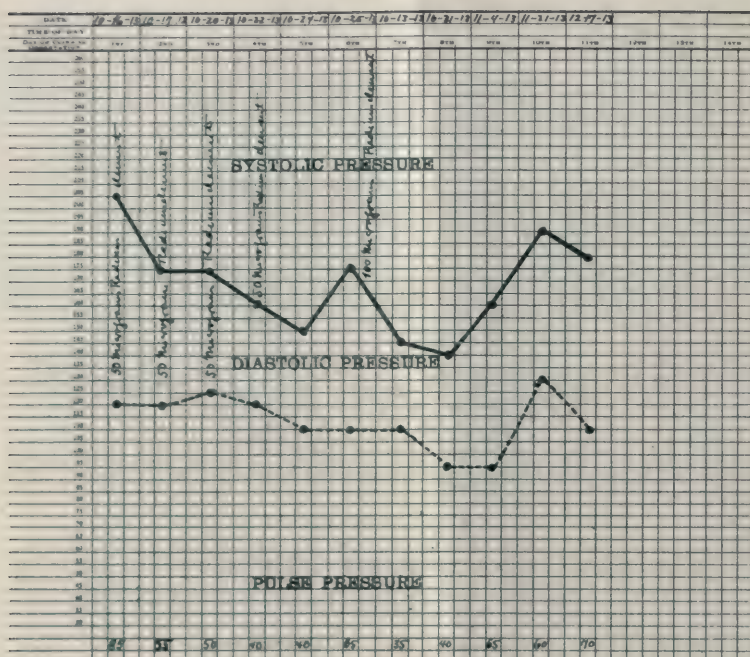
CASE No. 5—Male, Age 70 Years.

Right and left ventricle of heart slightly enlarged. Marked sclerosis of peripheral vessels. Few granular casts, but no albumen, in the urine.

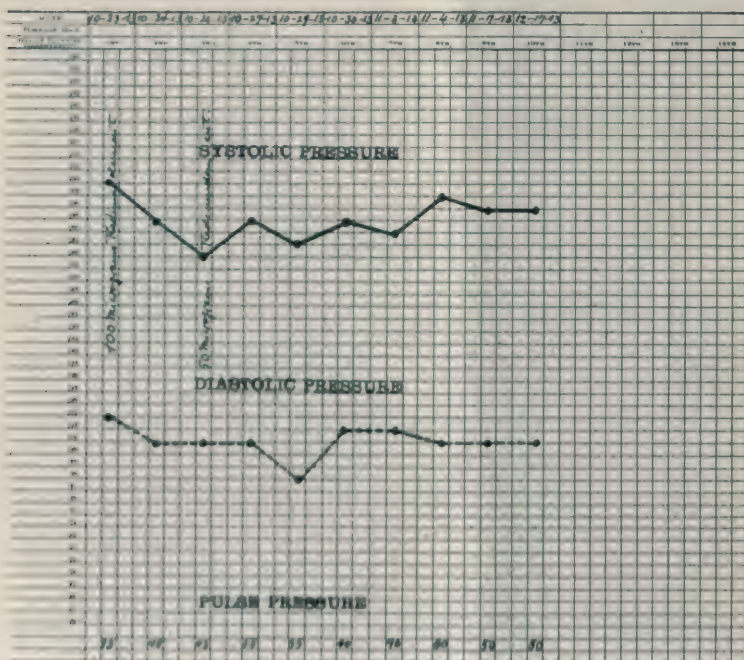
Date	Systolic	Diastolic	Pulse Pressure
10-16-13	205	120	85
	50 micrograms radium element intravenously.		
10-17-13	175	110	65
	50 micrograms radium element intravenously.		
10-20-13	175	125	50
	50 micrograms radium element intravenously.		
10-22-13	160	120	40
	50 micrograms radium element intravenously.		
10-24-13	150	110	40
10-25-13	175	110	65
	100 micrograms radium element intravenously.		
10-30-13	145	110	35
10-31-13	135	95	40
11- 4-13	160	95	65
11-21-13	190	130	60
12-17-13	180	110	70



Blood Pressure Chart Case No. 4.



Blood Pressure Chart Case No. 5.



Blood Pressure Chart Case No. 6.

After giving 200 micrograms radium element in divided doses of 50, 50, 50 and 50 the systolic blood pressure was reduced from 205 mm. to 150 mm. at the end of the eighth day. On 10-25-13 there was an increase to 175 mm., and at this time 100 micrograms of radium element was given. Again the pressure remained the same for a period of four days, following which there was a decrease, reaching its lowest point, 135 mm., on 10-31-13, being 70 mm. lower than at the beginning of observation. From this time there was a gradual increase to 190 mm. on 11-21-13. The final examination on 12-17-13 showed a systolic pressure of 180 mm., being a total reduction of 25 mm. The diastolic pressure showed a reduction at the end of the first eight days from 120 mm. to 110 mm. The lowest reduction was on 10-31-13, being 95 mm., increasing again on 11-3-13 to 125 mm. and declining again to 95 mm., again increasing to its highest point, 130 mm., 11-21-13. Final examination on 12-17-13 showed 110 mm., being only 10 mm. lower than at the beginning of observation. The lowest pulse pressure, 35 mm., was noted on 10-30-13, the final reduction, 12-17-13, being only 15 mm.

CASE No. 6—Male, Age 60 Years.

Sclerosis of peripheral vessels. No albumen or casts in the urine.

Date	Systolic	Diastolic	Pulse Pressure
10-23-13	170	95	75
100 micrograms radium element intravenously.			
10-24-13	150	105	45
10-25-13	140	95	45
50 micrograms radium element intravenously.			
10-27-13	170	115	55
10-29-13	165	110	55
10-30-13	160	120	40
11- 3-13	180	110	70
11- 4-13	165	105	60
11- 7-13	165	115	50
12-17-13	140	90	50

After the injection of 100 micrograms radium element the systolic blood pressure was reduced from 170 mm. to 140 mm. after a period of three days. After the injection of 50 micrograms more of radium element there was an increase of systolic blood pressure to 170 mm. On 11-3-13 the systolic pressure was 180 mm. and at the time of last observation, 12-17-13, 140 mm., being a total reduction of 30 mm. The diastolic blood pressure did not show any decrease following the radium injections, but gradually increased to its maximum, 120 mm., on 10-30-13, and on final examination, 12-17-13, was found to be 90 mm., being only a total of 5 mm. The pulse pressure was lowest 10-30-13, being 40 mm., and was 50 mm. on 12-17-13, being a total reduction of 25 mm.

CASE No. 7—Male, Age 50 Years.

Excessive drinker. Tremendously enlarged heart, both left and right ventricle. Apex in sixth intercostal space. No murmurs. No albumen in urine. Adipositas.

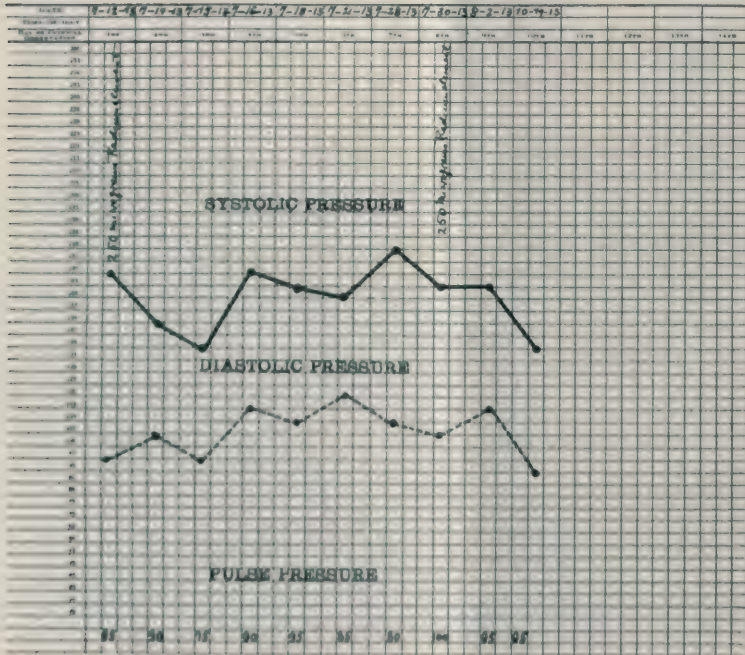
Date	Systolic	Diastolic	Pulse Pressure
7-12-13	210	115	95
250 micrograms radium element intravenously.			
7-14-13	195	105	90
7-15-13	180	105	75
7-16-13	195	105	90
7-18-13	185	90	95
7-21-13	195	110	85
7-28-13	190	110	80
7-30-13	205	105	100

250 micrograms radium element intravenously.

8- 2-13	200	105	95
10-19-13	200	105	95

The systolic pressure after injection of 250 micrograms radium element was reduced within three days from 210 mm. to 180 mm. There was a gradual increase during the next 16 days up to 205 mm. After the second injection of 250 micrograms a reduction of 5 mm. was noted, and on final examination, 10-19-13, the systolic pressure showed only a total reduction of 10 mm. The diastolic pressure after the first injection was lowered 10 mm., reaching its lowest point 7-18-13, 90 mm., which was six days later, and gradually increased to 105, as noted on final examination, being a total reduction of 10 mm. The lowest pulse pressure was noted 7-18-13, 90 mm. The lowest pulse pressure was noted 7-18-13, 90 mm. The final observation showed no change in the pulse pressure.

(To be concluded in the next number.)



REVIEWS AND ABSTRACTS.

E. Bumm. Further Results with Radium Therapy in Carcinoma. *Berliner klinische Wochenschrift*, Vol. 51, pp. 193-8 (1914). A lecture delivered before the Berlin Medical Society, December 3rd, 1913. The author says he had nothing to retract from his former statements made before the Berlin Medical Society in 1912 and the Gynecological Congress at Halle in 1913, where he spoke of the splendid results of radium and mesothorium in the treatment of carcinoma. Without exception, in all of the 108 cases which so far have been treated for a sufficient length of time, there has been noted in the course of three to five weeks a local healing effect due to the action of the rays. Clinically the first effect observed is a condition of irritation. Nodules swell and become sensitive. The tumor shows an increased transudation and plethora. Generally in from 8 to 14 days there is a decrease in size and shriveling, nodules become sharply defined and harder as they diminish in size. The surface of the growth becomes clean, the carcinomatous tissue becomes more like normal granulation tissue, the discharge diminishes and becomes odorless; nothing can be abraded from the growth, and on cutting with a knife the impression is that of cutting hard cartilaginous tissue. Cancerous nodules leave the superficial skin intact and disappear without visible scars. In the case of more extensive growths there remains a thin induration, which superficially becomes a thin crust. In the course of time, sometimes weeks, sometimes months, the induration disappears, and then the last traces of the original cancerous growth have disappeared.

Microscopically this change consists in the destruction of the cancer tissue, consisting in changes in the cell, the decay of the nuclear substance, cessation of mitosis and the disintegration of the protoplasm. Together with this there is a fibrous and hyaline degeneration of the connective tissue, and finally in the induration there is nothing but a few layers of undifferentiated masses which were carcinomatous nests. These results are splendid, and in spite of the voices which have been lately raised saying that the well-known caustics and the cautery are in the same class, and speaking of a "radium intoxication," and a great deception, it must be emphasized that the local action of the rays on carcinomatous tissue is wonderful, and this fact will remain no matter what the final decision may be.

There is nothing in our store of remedies with which it can be compared. There is a great difficulty which still must be surmounted. The local destruction of the cancer tissue is not enough. To secure permanent cures the effects must extend from the seat of the primary lesion out to the metastases, and in this bad effects on normal tissue must be avoided. These last are most difficult points, and here is where further work must be done. The dangerous secondary effects must be considered, particularly since most workers have not rayed patients sufficiently to obtain these effects, and others having observed the effects have failed to describe them. In advanced cases, to obtain results in some depth of tissue, large quantities of radioactive substances are applied for long periods. In such cases after the scab formation there is a slow change, some-

times in one to two months, often after a quarter or half year, which involves all the tissues that has been rayed. For some reason these changes take place long after the raying and they may make all the results questionable. Until recently, particularly from microscopic pictures of the rayed tissue, there has been assumed a specific selective action of the rays on carcinoma cells.

According to *Bumm's* opinion the rays do not act qualitatively, but only quantitatively, in a different manner on carcinomatous and muscle tissue. The rays act more strongly and rapidly on the delicate young cells of the rapidly growing neoplasm, so that they are more readily damaged than the connective tissues. However, the damage to the more resistant tissues is only much slower and comes into evidence later. This change coming on a half year later at first led to the thought of recurrences. However, excised bits showed no trace of cancer nests, and in general there was simply a hyaline degeneration of the connective tissue; muscle fibers, vessels, fascia—all become part of the induration. This change which the radiations bring about may be favorable as preventing the later development of cancer nests that may remain. However, where there are adjacent body cavities, separated by thin septa, indurations may lead to strictures, and in the case of hyaline degeneration fistulas and perforations may result.

There is danger particularly where the carcinomatous infiltrations have involved the bladder or rectum. Advanced cases in which there is such involvement are treated with great caution. *Bumm* thinks the secondary rays from the lead filters and the gamma rays are the cause of the hyaline degeneration of the various tissues in which these rays penetrate. Small doses do not cause the change, but 200 to 300 milligrams of radium (bromide) used twice for periods of ten hours can begin to produce the effect.

The permanent results of such radium treatment can only be judged by observing the cases for years after the treatment, since it is always a matter of influencing the metastases which follow the glands and which must be sufficiently affected. After ray treatment which has removed the primary growth the patient is just in the same stage as one after a successful operation, when the wound has just healed. We have some idea of the permanency of results after operations since statistics have been secured. Such data must now be secured with regard to ray treatment.

After describing six cases of uterine carcinoma in which it was shown that all signs of the cancerous growth had disappeared, or at least there were only several small nests left in the resulting indurated tissue, *Bumm* says we may view the results as good or bad, accordingly as we look at them with an optimistic or a skeptical eye. As a result of the work on these cases he draws the following conclusions:

(1) The complete destruction of carcinomatous growths up to a depth of 2.5 cm. (measured on the contracted growth, which will be about 3 to 3.5 cm. from the surface of the cancer) can be effected with means available at present. The superficial area of the cancer is of less moment, since by a suitable arrangement of the radioactive preparations all parts of the growth can be rayed. However, in many cases there may be some part of the growth

upon which smaller doses of the rays strike, and here there will be isolated nests of cancer cells. Many may think 3.5 cm. a small range for the action of the rays. However, it is only the advanced cases of carcinoma of the cervix where the growth is thicker than 2 cm.

(2) At 4 cm. there is no longer the same destructive action on the cell and 4 cm. in the parametrium, in spite of massive doses, there have been found vigorous carcinomatous cells in groups as large as peas or cherries. Beyond 5 cm. the cancerous lymph glands are not at all affected.

Of the 108 cases which have been treated, 15 have had recurrences, and when it is considered that only 40 of all the cases were operable, this would be a splendid result, if the period of observation had been several years. However, it must be said that two-thirds of the cases have been under observation less than a half year.

Bumm concludes, in view of his experiences with massive doses, that 200 milligrams of radium (bromide) or its equivalent in mesothorium, is a large dose, and for usual doses recommends from 50 to 100 mgm. (*i. e.*, about 25 to 50 mgm. radium element). The later effects of huge doses in causing indurations and hyaline degeneration in the normal tissue are undesirable and unexpected rapid and extensive necrosis in these tissues may result if they are later subjected to the rays. Fever is a general symptom often noted after the use of massive doses of the rays. It may go as high as 40° C. With the fever there is a general weakness, poor appetite and a rapidly increasing anemia which persists even after the fever has subsided. The time of application must be governed by the amount of radium applied. Larger doses of several hundred milligrams should only be used for several hours. Average doses of 50-100 mgm. radium (bromide) may be used for from 6 to 12 hours without danger, but the local and general condition must always be kept in mind.

As regards screening *Bumm* says that he has given up the use of lead filters for two reasons. Along with the soft rays they absorb some of the penetrating rays, and also the secondary rays from lead screens are more penetrating, and these rays are undesirable since they cause most of the observed superficial burns. In place of the lead, brass (1.5 mm.) and aluminum (3 mm.) screens are now used with 2 mm. of metal free rubber to absorb the resulting secondary rays. After the first reaction had been observed it is best to not place the tube directly on the tissue, but to have it several millimeters above the growth, celluloid capsules or cotton covers serving for this purpose. This avoids the very intense action of the rays, which is, of course, greatest nearest the radium, the intensity of the radiations diminishing inversely as the square of the distance.

In conclusion *Bumm* states that he has always used the Roentgen rays in conjunction with the radioactive substances and, in view of the bad effects of the very massive doses, he prefers to use the radioactive substances to influence the local carcinomatous growth, using the penetrating X-rays on the neighboring tissues. In five operable cases of uterine cancer the X rays alone gave good

results, and in two inoperable cases one is locally healed, the other being considerably improved. *Bumm* predicts that in the future cancer will be treated by radiotherapy. Now growths of 3 cm. thickness can be influenced, and if improvements in the technic, etc., make it impossible to work a few centimeters deeper, then radiotherapy can do all that extensive surgical treatment could do, and often radiotherapy can lead to cures where operative treatment is out of the question. If there are no advances made over what can be done today, even then radiotherapy makes a good step forward in our fight on cancer.

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A. *Gunsett*. The Radium Treatment of Cancer of the Uterus in France. *Strahlentherapie*, Vol. 4, pp. 36-43 (1914). A lecture given at Strasburg before the Medical Society of Lower Alsace, November 8th, 1913. In view of the rather contradictory reports made at the several medical congresses, in regard to the value of radium in the treatment of cancer, the author reviews the work of the French in radium therapy. At the International Congress for Physiotherapy in Berlin and at the Congress of Gynecologists at Halle the view was that mesothorium was an agent for use in uterine cancers, without any need of surgery. However, at the eighty-fifth meeting of German Scientists and Doctors at Vienna the general attitude was very pessimistic and the value of radium and mesothorium in the treatment of cancer was questioned. However, in both cases the results presented were of too recent observation to justify general conclusions. The earlier results with radium in France were obtained on superficial growths, using unscreened preparations containing rather small quantities of radium. In 1907 *Dominici* made an important step in advance in using filters of about a half millimeter thickness of lead, gold or silver, the irritating secondary rays from the metal being absorbed in paper or gauze. The rays which penetrate such screens have only about 8% of the activity, but their action on malignant growths is more intense, and their effects on normal tissue is far less intense. By use of these ultra penetrating rays superficial lesions could be influenced with less action, and even deep-seated growths could be affected. The time of application of the radium preparations was increased without producing dangerous effects. *Wickham* and *Degrais* used filters up to a thickness of 2 and 3 mm. of lead, thus securing a pure gamma radiation with only a small fraction of the hardest beta rays. However, these workers still used small quantities of radium, and took a very conservative stand. Their idea was that the role of radium was to assist surgery, or to make inoperable growths operable. In 1910 *Cheron* and *Rubens-Duval*, working in *Dominici's* laboratory, went a step farther in using heavy filters and large quantities of radium, applying massive doses.

Their conclusions in 1910 were that inoperable cancers of the uterus and vagina should be treated by the ultra penetrating rays, using massive doses and heavy screening. They recognized the bad effects of too small quantities of radium. Their work showed that the action of radium alone was sufficient to destroy the carcinomatous tissue in two cases of inoperable carcinoma of the uterus. The

results on 158 cases, treated according to their technic of massive doses, may be summarized as follows: One case cured; 77 cases, a complete disappearance of all the clinical symptoms and the patients apparently cured (46 of these with no recurrence after a year); 31 cases, local improvement or improvement that did not last; 12 cases, the improvement made operation possible; and in the remaining cases the carcinoma was so extensive that radium could only be considered as a palliative. *Cheron* and *Rubens-Duval* advise a combination of radium treatment with surgical interference. Certain types of cancerous growths may fall wholly within the domain of radium therapy, and in others surgical treatment is best, but a combination of radium and surgery is most advisable.

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Julius Stoklasa. The Significance of Radioactivity in Physiology. *Strahlentherapie*, Vol. 4, pp. 1-18 (1914). An address presented at the eighty-fifth meeting of German Scientists and Physicians at Vienna. The motive of the author's researches has been to discover the action of radioactive matter upon the process of metabolism in plant cells containing chlorophyll and those not containing chlorophyll. Native radioactive minerals were used (nasturan, containing 0.00013 gm. radium per kilo, and the pitchblende residues, containing 0.000396 gm. radium per kilo of material), radioactive water from the springs of St. Joachimsthal (300-600 mache units per liter), Franzenbad (150 m. u. per l.) and Brambach (1,700-2,000 m. u. per l.). These radioactive spring waters also contained thorium and actinium emanation. Further water was made radioactive by use of the emanation from a radium barium chloride preparation containing 5 mgm. of radium. Experiments were made in special culture media in flasks with bacteria (*azotobacter-chroococcum*) which assimilate nitrogen from the air, converting it into organic nitrogen. These experiments showed clearly that the growth of the bacteria in the presence of a concentration of 80 to 150 mache units per liter is accompanied by an increased (32-76%) nitrogen fixation. The beta and gamma rays were found to act unfavorably, causing the bacteria to grow more slowly, the amount of nitrogen fixation being diminished. Soil in large vessels (85 liters) was then exposed to the action of radium emanation, and it was clearly demonstrated that nitrogen assimilation in the presence of emanation was higher than in the control vessels containing no emanation. The radium emanation increases the synthetic processes and it retards the reduction of nitrates to nitrogen. Radium emanation is a concentration of 100 to 200 m. u. per liter, acts on yeast cells and the alcoholic fermentation process, markedly increasing the action of the cells. The effect of the presence of radium emanation on the action of the glucolytic enzymes, zymase, laktazidase and peroxydase is being further studied, but preliminary work shows that the physiological oxidation process is accelerated in the presence of the emanation.

In studying the action of radium emanation on higher plants the germination of seeds was first investigated, and it was found that a small concentration of radium emanation (100 seeds in small vessel with 50 c. c. water, containing a concentration of 15 to 30 m. u. per liter) has an accelerating effect upon the germination process. However, this effect varied with different sorts of seeds.

When the concentration of emanation was increased to 50 m. u. per liter the germination process began to be retarded. The natural radioactive spring waters were found to have a more energetic action on the seeds than the water made radioactive by passing radium emanation through it. This difference may be due to the natural waters also containing thorium and actinium emanation in addition to the radium emanation. The action of radioactive water on the cell increase and the growth of plants was studied, and it was found that in the presence of the emanation (96 m. u. in the vessel in which the plant was growing, size not stated) there was a great increase in dry weight of the plants which had been exposed to emanation during 46 days' growth, as the following table shows:

	Radioactive water.	Non-radioactive water.
<i>Pisum arvense</i>	6.873 gm.	2.137 gm.
<i>Vicia faba</i>	12.887 gm.	6.009 gm.
<i>Lupinus angustifolius</i>	3.793 gm.	1.845 gm.
<i>Hordeum distichum</i>	9.085 gm.	0.906 gm.

Other similar experiments on lentils, peas and wheat showed that by the use of radioactive water of 70 m. u. per liter there was an increase of from 62 to 158% in the dry weight of the plants over the dry weight of control plants. When the concentration of emanation was increased the first effect was an increased growth, but above a certain concentration the effect of the emanation is to retard growth, as is shown in the following table of results using buckwheat:

	Dry weight plant.
Inactive water	9.45 gm.
Water containing 30 mache units.....	13.54 gm.
Water containing 60 mache units.....	19.54 gm.
Water containing 300 mache units.....	Bad effect noticeable

The effect of radioactive minerals on the growth of plants was tried, but these experiments are not yet complete, and as far as they go they show that a small amount of radioactive matter will cause an increased plant growth.

The effect of radium emanation upon the breathing of plant cells, i. e., the mechanism of physiological oxidation, was investigated, and it was found that under the influence of emanation in small concentrations (150 to 300 m. u. per liter of air) there is a great increase in the excretion of carbon dioxide and an increase in the amount of oxygen taken up. This increase amounted to from 32 to 66%. A short exposure to concentrations of 50,000 to 60,000 m. u. per liter had no apparent effect on the plants, although the longer action of a high concentration had a bad effect on the plants. The roots were found to be most resistant to the action of the emanation, and the seedlings and young leaves were most sensitive. The chlorenchyma with the chloroplasts of the older leaves was also affected by the strong radioactivity.

It was found that when plants were acted on by emanation of from 150 to 160 m. u. per liter there was a greater amount of carbon dioxide given off in daylight than at night. The control plants, without emanation, gave off more carbon dioxide than those subjected to emanation. This difference is due to the increased assimilation of the carbon dioxide. Using 466 milligrams of radium chloride *Stoklasa*, *Sebor* and *Zdobnický* were able to prepare a hexose by the action, for 56 hours, of radium emanation on carbon dioxide, nascent hydrogen in the presence of potassium hydroxide.

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